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Entrainment of Stage 2 Sleep Spindles by Weak, Transcerebral Magnetic Stimulation in an "Epileptic" Woman

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The proportions of Stage 2 spindles present per second over the prefrontal and temporal lobes of a patient who had been experiencing complex partial epileptic-like experiences and disturbances in sleep patterns for four years following a closed head injury were measured while a weak (1 microT) burst-firing magnetic field was applied transcerebrally through the temporoparietal regions. In several successive segments during the exposure the onsets of the spindles were significantly correlated (rhos between 0.30 and 0.40) with the onset of the field that was presented once every 3 s for about 0.7 s. Lag/lead analyses indicated only the contemporary occurrence of the fields and the spindles were significantly correlated over time. These results suggest that some states of consciousness, particularly those associated with the "epilepsy spectrum disorder" may be more sensitive to entrainment or "synchronization" by weak complex magnetic fields whose temporal structures are designed to simulate natural brain activity.

Keywords Electroencephalogram; Entrainment; Complex magnetic fields; Temporal lobe; Stage 2 sleep; Spindles; Head injury.

Introduction

Sensitivity to weak complex magnetic fields during more altered states of consciousness for individuals whose brains have been influenced by mild head injuries has not been explored. This probability is enhanced because many of these patients also display many of the subjective experiences of patients with partial complex epilepsy as defined by psychometric inventories (Roberts et al., 1992). That the epileptic brain is sensitive to weak magnetic fields is suggested by the lowered threshold for convulsions in rats (Bureau and Persinger, 1995) and human patients (Keshavan et al., 1981) during enhanced geomagnetic activity that can be simulated experimentally (Michon and Persinger, 1997). Interictal epileptiform activity was modified in more

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than half of the patients diagnosed with partial complex epilepsy with drug-resistant mesial temporal lobe foci by cerebral application of weak magnetic fields within the 1 milliTesla range (Dobson et al., 2000a, 2000b).

One mechanism by which weak, complex magnetic fields could affect behavior is by the entrainment of intrinsic phasic processes generated by the brain. Persinger et al. (1997) reported brief entrainment of electroencephalographic activity during transcerebral application of weak, complex magnetic fields. However the "entrainment" required the successive application of several different patterns of fields and involved normal volunteers who remained awake as defined by concurrent electroencephalographic activity between Stage 0 and Stage 1.

During the last 15 years, our laboratory has interviewed dozens of patients who have sustained head injuries, often not associated with any apparent suspension of consciousness. These patients have reported their subsequent increased subjective sensitivities to the electromagnetic fields generated by electronic devices such as computers and televisions. Their reports have been usually dismissed as "crazy" by others. Most of these patients were also diagnosed with fibromyalgia or myalgic encephalomyelitis (chronic fatigue).

In previous studies, Baker-Price and Persinger (1996, 2003) showed that transcerebral applications of weak (1 microTesla) burst-firing magnetic fields presented once every 3 s for 30 min once per week for 6 successive weeks reduced depression for patients who had sustained "mild" closed head injuries. The treatments resulted in a significant improvement of mood as defined by both norm-referenced psychometric tools and subjective reports, reduction in complex partial epileptic-like signs and shifts towards faster (beta) frequencies within electroencephalographic power spectra.

This case study examines the relationship between weak complex magnetic fields on the electroencephalographic (EEG) activity during a shift in consciousness (e.g., Stage 2 sleep) of a patient who had previously suffered a closed head injury. The hallmark of this stage is the frequent but intermittent approximately 1 s bursts of 13–15 Hz paroxysmal activity that have been labeled "sleep spindles" (Niedermeyer and Lopes da Silva, 1987). These patterns first appear over the vertex and appear to reflect the activity of the most posterior portion of the supplementary motor area, a region frequently associated by neurologists with complex partial seizures as well as with psychogenic seizures or pseudoseizures. The results of the present experiment suggest that sensitivity to entrainment by weak complex magnetic fields may be enhanced during the early stages of suspension of normal consciousness when a person enters Stage 2 sleep.

Patient and Methods

The patient was between 45 and 50 years of age. She had been involved in a motor vehicle incident (head-on collision) about four years before the treatment. Since the injury she had been diagnosed with whip-lash injuries and fibromyalgia. The subject had been divorced before the injury and had no children. At the time of the treatment she was experiencing difficulty sleeping. Her medications included Advil (ibuprofen), Flexeril (cyclobenzaprine hydrochloride), Paxil (paroxetine hydrochloride), and Elavil (amitriptyline), as well as specialized medication for Crohn's disease. The patient had been referred by a specialist because of the long history of difficulties with adaptation following the injury and because of the failure of conventional pharmacological agents

to eliminate the distress. There was no formal history of overt seizures. However, her score for Roberts' Epilepsy Spectrum Disorder (Roberts et al., 1992) was four standard deviations above the normative mean.

During the measurements the patient sat within a comfortable chair that was housed within an acoustic chamber. She was blindfolded and asked to relax. She was cognizant of her option to stop the experiment at any time. During the procedure, bipolar activity was recorded by a Grass P79 instrument from silver-silver flat disc electrodes held by EC2 cream on the scalp between the prefrontal (F7–F8), temporal (T3–T4), and occipital (O1–O2) lobes. For the first five minutes the activity was monitored without the application of the treatment.

During this period, the patient displayed alpha dropout and the occurrence of classic Stage 2 spindles over the prefrontal and temporal regions. The field was then activated. It consisted of a complex, burst-firing magnetic field presented transcerebrally through the brain once every 3 s. The duration of each pulse was 690 ms and the duration of each point that composed the pulse was 3 ms. The strength of the field was about 1 microTesla along the inside edge of the lateral sides of the helmet through which the fields were delivered. They were generated by a cluster of four solenoids on both sides of the helmet that were embedded in plastic at the approximate level of the temporal lobes. Each of the four pairs (one of the left and one on the right) was activated for 0.5 s such that rotation through the four pairs occurred once every 2 s. More detailed descriptions of the apparatus have been reported elsewhere (Baker-Price and Persinger, 2003; Richards et al., 1993).

Quantitative assessment of the record was completed by the first author. The presence or absence of the applied field as well as the presence or absence of a spindle complex within the prefrontal and temporal measurements were indicated by a 0,1 score for each of the 440 successive s of the field's application. If the duration of a spindle exceeded 1 s then the value 1 was give only to the first second in which the spindle occurred. The signature from the induction produced by the field had been superimposed upon the activity over the occipital region. This allowed a precise measurement of the presence and absence of the field with respect to the presence or absences of spindles.

The data were loaded for computer analyses such that each second was a case and the presence and absence of the field or the spindles were variables. To discern internal consistency, the sequences of data were analyzed in 6 separate segments each containing 80 s. This value was selected for convenience because at our paper speed (15 mm/s) 80 s is 4 segments of paper.

Spearman (rho) correlations were completed between the presence or absence of a spindle in the records for temporal and prefrontal regions and the presence or absence of the field during the same second or for each of the previous five seconds. This was accomplished by employing five separate lag variables. To accommodate for possible "lead" effects, five separate lag variables were calculated for the presence or absence of spindles for each of the two pairs of lobes. To insure that an intrinsic 3 s periodicity was not present within the occurrence of the spindles (and hence would lead to spurious correlations with the timed presence and absence of the field), partial correlation analyses were completed.

The correlations between the presence or absence of spindles over the temporal and frontal lobes and the presence or absence of the field during the same second or each of the previous 5 s were completed. The residual correlations, after the shared variance with the presence or absence of a spindle 4 s previously (lag 4) or 3 s previously

(lag 3) had been removed, were also calculated. All analyses involved SPSS software on a VAX 4000 computer.

Results

The percentages of seconds that contained spindles over the frontal or temporal lobes and the percentages of seconds the fields were present during the period of measurement are shown in Table 1. The mean for the proportion of seconds containing the onset of the field was 0.276 s which is equivalent to a field presentation about every 3.6–3.7 s which is the time of the interstimulus interval (3 s) plus the duration of the burst-pattern (690 ms). There were no statistically significant correlations between the occurrences of a spindle in a second and the occurrences of a spindle in the previous first, second, third, or fourth second over either the prefrontal or temporal lobes (all rhos between −.10 and .10) during period 1 when no field was present.

The results of the correlation analyses between the occurrence of a spindle over the temporal and prefrontal lobes and the presence of the field for each of the five successive segments in which the field was being presented are shown in Table 2.

Table 1
Percentage of seconds during each 80-s observation period when Stage 2 sleep spindles were present over the frontal and temporal lobes and the burst-firing magnetic field was present

Increment	Frontal spindles	Temporal spindles	Field presence
1	20	15	00
2	13	09	26
3	34	24	26
4	31	24	28
5	31	24	30
6	25	25	28

Table 2
Correlation coefficients between the presence of spindles and the presence of the field over the prefrontal and temporal region and after the shared variance with the occurrence of spindles 3 or 4 s before have been accommodated

	Prefrontal lobes			Temporal lobes		
	rho partial			rho partial		
Segment		3 s	4 s		3 s	4 s
2	.29*	.30*	.29*	.32*	.31*	.29*
3	.30*	.31*	.31*	.27*	.28*	.29*
4	−.01	−.05	−.04	−.05	−.04	−.05
5	.33*	.32*	.32*	.28*	.30*	.32*
6	.44*	.45*	.45*	.45*	.44*	.44*

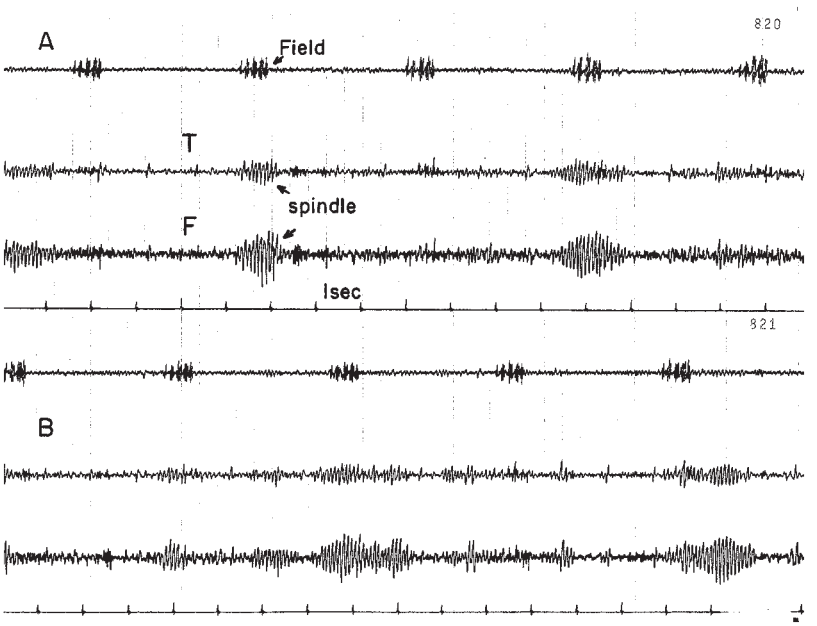

Figure 1. Graphic relationship between the presentation of the burst-firing field registered on the first channel (superimposed upon the occipital measurements) and the occurrence of spindles (Stage 2) over the temporal (T) and frontal (F) lobes for 40 successive s (panel A,B).

Because there were no significant correlations ($p > .05$) between any of the five lags or leads, only the contemporary (same second) results are given. The values for the partial correlation coefficients, after the shared variance with the presence or absence of spindles 3 s and 4 s previously, are also shown.

The numbers of times spindles occurred when the field was present were significantly ($p < .05$) correlated during the same second for four of the five, 80-s segments for both the temporal and prefrontal lobes. Partial correlations between this concordance, when occurrences of spindles during three or four seconds were held constant, did not alter this relationship. A sample of the strip chart is shown in Figure 1. The correlations between the presence or absence of spindles between the prefrontal and temporal regions for each of the six segments ranged between 0.78 and 0.96.

It may be of interest that before the first session, the patient required, because of the pain produced by walking, a wheelchair to enter the laboratory. Before the second session, one week later, she arrived using only a walker, while before the third session she required only a cane. She reported the pain in her neck and back had subsided significantly after the first treatment. However, the intensity of the pain returned, according to her reports, within about 30 d after the last treatment.

Discussion

This single case study suggests that a weak complex, burst firing magnetic field presented every 3 s while the person entered Stage 2 sleep may have partially entrained or "synchronized" the timing of the sleep spindles. We infer "partial"

entrainment because the correlation coefficients were not stronger and because one of the six, 80-s increments of analysis did not display the relationship. Although the interstimulus intervals of the field were fixed by experimental design, the inter-response time of the spindles were not. There was no evidence of a periodicity within the range of 1–4 s for the occurrence of spindles over the prefrontal or temporal lobes when the field was not present.

In addition, if a quasi-regularity had occurred, then there should have been significant correlations between the various lag variables computed for the presence or absence of the field and the occurrence of the onset of the spindles. This relationship was not observed. The significant correlation occurred only for the same-second intervals in which the field had been activated.

The reason for the lack of relationship between the presence of spindles and the presence of the applied field during segment 4 remains to be elucidated. It is possible that there is some cyclical or phase-shifting component that will require longer exposure times and additional experiments to be seen. In addition, since the subject was separated from the experimenter and not visible, it is difficult to discern if the patient herself was doing something different during that segment compared to the others. There were no obvious differences in the quantity or quality of sleep spindles during that segment which makes it unlikely that the subject had awoken or was shifting into another phase of sleep.

The possibility that the appropriate temporal and spatial structure of weak electromagnetic fields could affect levels of consciousness and entrain electroencephalographic alpha activity had been suggested decades ago by E. Stanton Maxey (personal communication). Other researchers, employing more elaborate technologies, have shown strong evidence for this possibility. For example, Subrahmanyam et al. (1985) reported that field strengths of a few nanoTesla, similar to pc 1 (continuous pulsations) phenomena generated within the earth's magnetic field, could affect the electroencephalographic records of waking volunteers. To our knowledge, this present case may be the first obvious example of the direct effects of a weak magnetic field upon the bursting of spindles in real time. Obviously, considering the numbers of medications that were being consumed by the patient, our observation may be valid only within specific conditions where synergisms between the patient's medication, type of brain injury, and the applied field are created.

The regions within the brain through which entrainment of spindles might occur cannot be deduced from our data. There is likely to be multiple sources for sleep spindles. They first emerge normally over the prefrontal regions. Depth recordings from epileptic patients have shown the initial emergence of spindles within the orbital cortex and the more ventral gyri of the inferior frontal lobes. Depth recordings within the thalamus of patients displaying chronic pain have revealed independent thalamic spindles originating from the ventrobasal complex (Niedermeyer and Lopes da Silva, 1987).

Regardless of the source, the functional shift in neuronal activity during Stage 2 appears to be related to changes in the firing of thalamic neurons from a tonic or continuous pattern to a burst mode that is associated with hyperpolarization of the cell membrane. The latter consists of a few spikes between 250 and 400 Hz that recur with the waxing-and-waning spindles (Barlow, 1993). It may be of interest, although not necessarily causal, that the duration for each of the points (voltages) that comprised our burst-firing field was 3 ms whose frequency equivalence would be approaching 330 Hz. Theoretically, the generation of the first few 3 ms points of the

burst-firing pattern with different strengths by the computer could have satisfied the condition of a ''few spikes'' between 250 and 400 Hz.

It may be relevant that high-frequency oscillations of 250–500 Hz, termed ''fast ripples'', have been measured in seizure-generating limbic areas in rats in which epilepsy has been induced experimentally and in patients with mesiobasal temporal lobe epilepsy (Bragin et al., 2002). Their occurrence appears to reflect hypersynchronous events within epileptic zones within the entorhinal cortices that in turn may provide input to other brain areas. Via a remarkable cascade of corticocortical projections, inputs from the entire cortical mantle converge on the superficial layers (II and III) of the entorhinal cortices (Alonso and Klink, 1993). Outputs from these layers target important subcortical limbic centers, such as the amygdala, and are the origin of the perforant pathway, the major cortical afferent projection to the hippocampal formation.

That endogenous oscillators within the brain are uniquely susceptible to field-mediated perturbations has been shown by Liboff and his colleagues (Jenrow et al., 1998). They found that a 16 Hz, approximately 30 microTesla magnetic field externally applied for 60 min to urethane anesthetized rats attenuated rhythmic slow wave (theta) activity in the hippocampus. This consequence of synchronous bursting among pyramidal neurons was replaced by large irregular-amplitude activity that persisted for up to 90 min after the termination of the exposure to the field. These authors hypothesized that the disruption of rhythmic slow wave activity could still be accommodated by Faraday-induced electric fields, even if the calculated values were more than a million times less (10^{-7} mV/m) than those putatively associated with endogenous field effects (about 1 mV/mm), if the detection was mediated by mechanisms involving larger spatial domains within the hippocampus.

Sandyk and Anninos (1992) reported that seizure activity in epileptic patients could be attenuated by external application of very weak, complex magnetic fields. Some patients with partial complex seizures responded very well. If the temporal and spatial configurations of the fields employed by Anninos et al. (1991) and Sandyk and Anninos (1992) interfered with the mechanisms by which the fast ripples were hypersynchronized, particularly within the middle layers of the entorhinal cortices where these ripples exhibit a reversal in polarization, then more precise ''tuning'' of these complex fields could prevent the hypersynchronization from ever occurring.

The involvement of high-frequency oscillations in the mediation of weak complex magnetic field effects may be relevant to large populations of patients who sustain impacts of substantial mechanical energy to their brains, even without the loss of consciousness (Persinger, 1993, 1995a, 1995b). More than three-quarters of these patients show marked elevations of the incidence and intensity of symptoms that comprise the Epileptic Spectrum Disorder (Roberts et al., 1992) Although these patients do not display epileptic seizures as defined by classical definitions, the ''neuroelectrical noise'' (Roberts et al., 1990) and concomitant subjective experiences are very similar to patients with diagnosed partial complex seizures with foci in the temporal lobes (Persinger and Makarec, 1993).

If this ''electrical noise'' is being generated from the entorhinal cortices, then the successful treatment, by the type of field employed in this study (Baker-Price and Persinger, 1996, 2003) of depressed patients who have sustained these head injuries and who do not respond to antidepressant medications may interfere with the ''subclinical'' hypersynchronization spreading to other cortical areas. This potential treatment is important because about 20–30% of epileptic patients display epilepsy

that is difficult to treat by traditional pharmacological agents. About 80% of these drug-resistant epilepsies involve foci within the entorhinal cortices, hippocampus, or amygdala (Heinemann et al., 1993).

For some biophysicists the idea that weak complex fields could significantly influence the aggregate produced by the billions of neurons within neocortex and compensate for thermal agitation at biological temperatures is not sensible. However, we suggest that during shifts in states of consciousness the information within weak, complex magnetic fields may be more effective than during more stable states such as waking, slow wave sleep, or even rapid eye movement (REM) sleep. This concept would be similar to the basic principle in physics that weak forces and subtle energies can affect systems during periods dominated mathematically by derivatives or physically by rapid changes in states or boundary conditions. Within the physical world, such as during a martial arts competition, re-directing a back kick moving towards the experient requires much less energy than either its initiation or sudden termination by a block.

During these brief periods, when changes in state occur, information might be represented within the brain. Once represented within brain, the information could be more easily incorporated as the normal content of neuronal memory. One extrapolation of this assumption would be the ''re-setting'' of desynchronized groups of neurons that had been responsible for normal function. A single exposure for 30 min indicates that the patient's brain was exposed to 500 presentations of the fixed interval of burst-firing. Whether or not this number is sufficient to induce the required ''re-synchronization'' within neurons requires more experimentation.

This case study furthers our understanding of how externally applied weak complex magnetic fields can influence brain activities and provide insight into conditions and methods by which these fields may be best applied. The importance of understanding the potential of weak complex magnetic fields as a treatment for epilepsy cannot be underestimated as nearly a third of all sufferers are non-responsive towards traditional pharmaceutical interventions. As humans are continuously immersed in electromagnetic fields, researchers and clinicians must fully appreciate their putative impact on patients and treatments.

Declaration of Interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

Alonso, A., Klink, R. (1993). Differential electroresponsiveness of stellate and pyramidal-like cells of medial entorhinal cortex Layer II. *J. Neurophysiol.* 70:128–143.

Anninos, P. A., Tsagas, N., Sandyk, R., et al. (1991). Magnetic stimulation in the treatment of partial seizures. *Int. J. Neurosci.* 60:141–171.

Baker-Price, L., Persinger, M. A. (1996). Weak, but complex pulsed magnetic fields may reduce depression following traumatic brain injury. *Percept. Motor Skills* 83:491–498.

Baker-Price, L., Persinger, M. A. (2003). Intermittent burst-firing weak (1 microTesla) magnetic fields reduce psychometric depression and complex partial epileptic-like signs in patients who sustained closed head injuries: A replication and electroencephalographic validation. *Percept. Motor Skills* 96:965–974.

Barlow, J. S. (1993). *The Electroencephalogram: Its Patterns and Origins*. Cambridge (Mass): The MIT Press.

Bragin, A., Wilson, C. L., Staba, R. J., et al. (2002). Interictal high-frequency oscillations (80–500 Hz) in the human epileptic brain: Entorhinal cortex. *Ann. Neurol.* 52:407–415.

Bureau, Y. R. J., Persinger, M. A. (1995). Decreased latencies for limbic seizures induced in rats by lithium-pilocarpine occur when daily average geomagnetic activity exceeds 20 nT. *Neurosci. Lett*. 192:142–144.

Dobson, J., St. Pierre, T., Wieser, H. G., et al. (2000a). Changes in paroxysmal brainwave patterns of epileptics by weak-field magnetic stimulation. *Bioelectromagnetics* 21:94–99.

Dobson, J., St. Pierre, T. G., Shultheiss-Grassi, P. P., et al. (2000b). Analysis of EEG data from weak-field magnetic stimulation of mesial temporal lobe epilepsy patients. *Brain Res*. 868:386–891.

Heinemann, U., Zhang, C. L., Eder, C. (1993). Entorhinal cortex-hippocampal interactions in normal and epileptic temporal lobe. *Hippocampus* 3:89–98.

Jenrow, K. A., Zhang, X., Renehan, W. E., Liboff, A. R. (1998). Weak ELF magnetic field effects on hippocampal rhythmic slow activity. *Exp. Neurol*. 153:328–334.

Keshavan, M. S., Gangadhar, B. N., Gautam, R. U., et al. (1981). Convulsive threshold in humans and rats and magnetic field changes: Observations during total solar eclipse. *Neurosci. Lett*. 22:205–208.

Michon, A. L., Persinger, M. A. (1997). Experimental simulation of the effects of increased geomagnetic activity upon nocturnal seizures in epileptic rats. *Neurosci. Lett*. 224:53–56.

Niedermeyer, E., Lopes da Silva, F. (1987). *Electroencephalography: Basic Principles, Clinical Applications and Related Fields* (2nd edn.). Baltimore: Urban & Schwarzenberg.

Persinger, M. A. (1993). Personality changes following brain injury as a grief response to the loss of sense of self: Phenomenological themes as indices of local lability and neurocognitive structuring as psychotherapy. *Psychol. Rep*. 72:1059–1068.

Persinger, M. A. (1995a). Clinical neurological indicators are only moderately correlated with quantitative neuropsychological test scores in patients who display mild-moderate brain impairment following closed-head injuries. *Percept. Motor Skills* 81:1283–1292.

Persinger, M. A. (1995b). Neuropsychologica principia brevita: An application to traumatic (acquired) brain injury. *Psychol. Rep*. 77:707–724.

Persinger, M. A., Makarec, K. (1993). Complex partial epileptic signs as a continuum from normals to epileptics. *J. Clin. Psychol*. 49:33–43.

Persinger, M. A., Richards, P. M., Koren, S. A. (1997). Differential entrainment of electroencephalographic activity by weak complex magnetic fields. *Percept. Motor Skills* 84:527–536.

Richards, P. M., Persinger, M. A., Koren, S. A. (1993). Modification of activation and evaluation properties of narratives by weak complex magnetic field patterns that simulate limbic burst firing. *Int. J. Neurosci*. 71:71–85.

Roberts, R. J., Gorman, L. L., Lee, G. P., et al. (1992). The phenomenology of multiple partial seizure-like symptoms without stereotyped spells: An epilepsy spectrum disorder? *Epilepsy Res*. 13:167–177.

Roberts, R. J., Varney, N. R., Paulsen, J. S., Richardson, E. D. (1990). Dichotic listening and complex partial seizures. *J. Clin. Exp. Neuropsychol*. 12:448–458.

Sandyk, R., Anninos, P. A. (1992). Magnetic fields alter the circadian periodicity of seizures. *Int. J. Neurosci*. 63:265–274.

Subrahmanyam, S., Sanker Narayan, P. V., Srinivasan, T. M. (1985). Effect of magnetic micropulsations on biological symptoms- a bioenvironmental study. *Int. J. Biometeorol*. 29:293–305.